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Japanese Published Examined Patent Application (Kokoku Koho), Application No. S45-51605, Filed June 16, 1970; Publication No. S48-17044, Published May 26, 1973; Int. Cl.: A61k 27/00 A23l 1/22 A23l 1/28; Inventor(s): Hiroshi Yoshino et al.; Assignee: Yamasa Soy Souse Corporation; Japanese Title: Iyakuhin no Nigami Jokyo Hou (Method for Eliminating Bitterness of a Pharmaceutical)

Detailed Description of the Invention

This invention is a method for eliminating bitterness of a pharmaceutical by adding uridylic acid (henceforth referred to as UMP) or cytidylic acid (henceforth referred to as CMP) and salts thereof (henceforth referred to as UMP-2Na and CMP-2Na) alone or by a mixture of two or more these compounds and bringing them into contact with it.

More specifically, pharmaceuticals that contain bitterness, mainly a crude drugs and organic chemical agents are formulated and processed or immediately before they are dosed, UMP or CMP and UMP-2Na or CMP-2Na are added to the pharmaceuticals alone or by a mixture of two or more compounds and then evenly mixed.

The crude drugs used for the invention refer to natural pharmaceuticals whose biochemical properties and pharmaceutical effect are studied, among Japanese and Chinese medicines and chemical agents including folk medicine used worldwide for a long period of time.

Organic chemical agents refer to organo-chamically synthesized pharmaceuticals. Many of these pharmaceuticals contain bitterness. Due to the bitterness, they are not easily dosed. For example, the following crude drugs are given: *senburi* (Japanese green gentian); gentiana; *rindo* (gentian); hydrochloric quinine; *oren* (goldthread); *kina* (cinchona); *tohi* (orange peel); *kyonin* (apricot stone); *daio* (rhubarb root); *kamitsure*

(chamomile); *nigaki*; *tokon* (ipecac); *mao* (mahuang). These are the following products of the organic chemical agents: Barubitaru (C8H12O3Na); Anti-pyrine (C11H12Ona); Akurinamin (C23H30ON3Cl2Hcl-2H2O); Acrynol (C18H21O4N3); Aminofirin (composed of a 2.8 to 14.1% ethylene diamine and a 78 to 83.5% raofirin); Prabitaru (composed of two molecules of amino pyrine and one molecule of berubitaru); kontoru (chlordifuzeperoxide); Finaline.

It has been an issue for a long time how to easily take pharmaceuticals that contain bitterness.

In order to eliminate the bitterness, the inventors studied in various ways. As a result, the inventors have found that the bitterness of these pharmaceuticals is eliminated or reduced by adding or contacting CMP or CMP-2Na or UMP or UMP-2Na or the mixture thereof to them. The present invention is finally attained as described above.

When the invention is carried out, these components can be added to the pharmaceuticals in the form of a formulated powder or to the pharmaceuticals immediately before they are dosed. These components can be also added to crude drugs when they are boiled or immediately before they are dosed after the boiling. The invention is described hereinbelow using the embodiments.

Embodiment 1

About crude drugs

After each crude drug at an amount for a one-day dose (Please see the detail description below) has been boiled by a heating means adding water at 600 ml, it is cooled to a normal temperature. CMP-2Na and UMP-2Na alone or a 1:1 ratio mixture

thereof are added to the supernatant at the following ratios at 0.1%, 0.2% and 0.3%. After sufficiently mixing the components, the bitterness of each testing solution is judged.

The measuring standard is defined as below:

++++...Extremely bitter

+++.....Very bitter

++.....Bitter

±.....Slightly bitter

-.....Not bitter

The results of the bitterness evaluation are indicated in Table 1.

Table 1

Name of pharmaceuticals	Adding concentration	Control group	CMP-2Na group	UMP-2Na group	CMP-2Na UMP-2Na=1:1
senburi	(Please refer to the original descriptions)				
rindo					
tohi					
kamitsure					
Gentiana					

The amount of each crude drug dosed per day is defined as below:

senburi.....0.15 g/day

rindo.....0.60 g/day

tohi.....3.00 g/day

kamitsure.....15.00 g/day

Gentiana.....0.50 g/day

Embodiment 2

About organic chemical agents

After distilled water at 300 ml has been added to and dissolved in each organic chemical agent at an amount for a one-day dose (Please see the detail description), a uniform solution is obtained. CMP-2Na and UMP-2Na alone or a 1:1 ratio mixture thereof are added to the solution at the following ratios at 0.1%, 0.2% and 0.3% so as to evaluate the bitterness. The same evaluation symbols as those as in Embodiment 1 are used.

The results of the bitterness evaluation are indicated in Table 2.

Table 2

Name of pharmaceuticals	Adding concentration	Control group	CMP-2Na group	UMP-2Na group	CMP-2Na UMP-2Na=1:1
Anti-pyrine	(Please refer to the original descriptions)				
Barubitaru					
Aminofilin					
Pirabitaru					
Control					
Fainalin					

The amount of each crude drug dosed per day is defined as below:

Anti-pyrine.....0.6 g/day

Barubitaru.....0.6 g/day

Aminofilin.....0.6 g/day

Pirabitaru.....0.6 g/day

Control.....0.03 g/day

Finalin.....0.12 g/day

As described above, the amount of uridylic acid or cytidylic acid and salts thereof alone or by a mixture of two or more these compounds added to the chemical solution prepared by adding water at 600 ml to each crude drug at the one day dose amount or the chemical solution prepared by adding water at 300 ml to each organic chemical agent at the one day dose amount is preferably 0.2% or greater.

The embodiments are described heareinbelow.

Embodiment 1

Dry *senburi* at 100 g is pulverized to obtain 80 meshes. A CMP-2Na powder at 800 g is added to the pulverized dry *senburi*. The powders are sufficiently mixed together. After water at 600 ml has been added to the *senburi* powder at 0.15 g/day, the water with the *senburi* powder is heated and boiled. When the boiled solution is dosed, the bitterness is low.

Embodiment 2

Dry gentiana at 100 g is pulverized to obtain 80 meshes. A CMP-2Na powder at 240 g is added to the pulverized dry gentiana. The powders are sufficiently mixed together. After water at 600 ml has been added to the gentiana powder at 0.5 g/day, the water with the gentiana powder is heated and boiled. When the boiled solution is dosed, the bitterness is low.

Embodiment 3

A UMP-2Na at 66 g and CMP-2Na at 66 g are added to an anti-pyrine powder at 100 g. The powders are sufficiently mixed together. After distilled water at 300 ml has been added to anti-pyrine at 0.6 g/day, anti-pyrine is sufficiently dissolved. When the anti-pyrine solution is dosed, the bitterness is low.

Embodiment 4

A CMP-2Na powder at 132 g is added to a Barubitaru powder at 100 g. The powders are sufficiently mixed together. After distilled water at 300 ml has been added to the Barubitaru powder at 0.6 g/day, the powder is sufficiently dissolved. When the Barubitaru solution is dosed, the bitterness is low.

Claim

A method for eliminating bitterness of a pharmaceutical by adding uridylic acid or cytidylic acid and salts thereof alone or by a mixture of two or more these compounds and bringing them into contact with it.

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1

⑤4医薬品の苦味除去法

⑵1特　　願　昭45—51605
⑵2出　　願　昭45(1970)6月16日
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発明の詳細な説明

本発明は苦味のある医薬品にウリジル酸(以下UMPと略称する)又はシチジル酸(以下CMPと略称する)およびそのナトリウム塩(UMP・2Na, CMP・2Naと略称する)の単独又は二種以上の混合物を添加接触せしめて苦味を除去する方法である。

詳しくは医薬品、主として生薬や有機薬品の苦味のある薬品を調剤加工するとき、又は服用する直前にUMP又はCMPおよびUMP・2Na又はCMP・2Naの単独又は二種以上の混合物を添加して均一に混合せしめる方法である。

本発明に用いる生薬とは和漢薬や世界各地で古くから用いられた民間薬を含む薬物のうち理化学的性質が明らかにされ薬理的な作用も研究されている天然物の医薬品を言う。

有機薬品とは有機化学的に合成された医薬品を言う。此等には苦味を有し飲みにくいものが多い。例えば生薬ではセンブリ、ゲンチアナ、リンドウ、塩酸キニーネ、オウレン、キナ、橙皮、キヨウニン、ダイオウ、カミツレ、ニガキ、トコン、マオウ等があり、有機薬品では例えば商品名で言うとバルビタール($C_8H_{12}O_3Na$)、アンチピリン($C_{11}H_{12}ONa$)、アクリナミン

2

($C_{23}H_{30}ON_3Cl2Hcl\cdot 2H_2O$)、アクリノール($C_{18}H_{21}O_4N_3$)、アミノフイリン(エチレンジアミン2.8～14.1%とラオフイリン78～83.5%からなる。)、ピラビタール(アミノピリン2分子、バルビタール1分子からなる。)コントール(クロルジフゼポキサイド)、フアイナリン等がある。

従来から此等苦味の多い医薬品をいかに飲みやすくするかに問題があつた。

本発明者等はかかる苦味を除去するために色々と研究した結果、此等の医薬品にCMP又はCMP・2Naもしくは UMP又はUMP・2Na或いは両者の混合物を添加接触せしめることにより、これら医薬品の苦味が除かれて、全く苦味がないか、苦味の少くなることを発見して本発明を完成した。

本発明を実施するに際しては此等医薬品を調整粉末としたものに添加するか、又は服用する直前に、又は生薬では煎じる時か、煎じて服用する直前に添加してもよい。以下本発明を実験例により示す。

実験例　1

生薬類について

各生薬1日服用量(但し書き参照)に600mlの水を加えて加熱して煎じた後常温迄冷却して、この上澄液に対してCMP・2Na, UMP・2Na単独又は1：1の混合物を上澄液に対して0.1%, 0.2%, 0.3%をそれぞれ添加してよく攪拌して各試験液の苦味を判定した。

測定の基準は次の如くである。

＋＋＋＋……ひどく苦い
＋＋＋……可成苦い
＋＋……苦い
＋……稍々苦い
土……微かに苦い
—……苦くない

苦味判定の結果は第1表の如くである。

3　　4

第　1　表

薬品名	添加濃度	対照区	CMP・2Na 区	UMP・2Na区	CMP・2Na UMP・2Na＝1：1
センブリ	0.1	++++	+++	+++	+
	0.2	++++	++	++	+
	0.3	++++	±	±	±
リンドウ	0.1	+++	+++	+++	+
	0.2	+++	++	++	+
	0.3	+++	±	±	±
橙皮	0.1	++	+	+	+
	0.2	++	±	±	+
	0.3	++	±	±	±
カミツレ	0.1	++	+	+	+
	0.2	++	±	±	±
	0.3	++	+	−	−
ゲンチアナ	0.1	++++	++	++	+
	0.2	++++	±	±	±
	0.3	++++	±	±	±

但し各生薬の1日の服用量は次の如くである。

センブリ……　0.15g／日
リンドウ……　0.60g／日
橙皮……　3.00g／日
カミツレ……　15.00g／日
ゲンチアナ……　0.50g／日

実験例　2

有機薬品について

各有機薬品1日服用量（但し書き参照）に300mlの蒸溜水を加えてよく溶して均一として、この溶液に対してCMP・2Na，UMP・2Na単独又は1：1の混合物を溶液に対して0.1％，0.2％，0.3％添加して苦味を判定した。判定の符号は実験例1と同様にした。

苦味判定の結果は第2表の如くである。

5　　6

第　2　表

薬品名	添加濃度	対照区	CMP・2Na区	UMP・2Na区	CMP・2Na＋UMP・2Na＝1：1
アンチピリン	0.1%	+++	++	++	++
	0.2	+++	+	+	+
	0.3	+++	±	±	±
バルビタール	0.1	+++	++	++	++
	0.2	+++	+	+	+
	0.3	+++	±	±	±
アミノフイリン	0.1	+++	++	++	++
	0.2	+++	+	+	+
	0.3	+++	±	±	±
ピラビタール	0.1	++++	+++	+++	+++
	0.2	++++	++	+	++
	0.3	++++	±	±	±
コントール	0.1	++++	+++	+++	+++
	0.2	++++	++	+	++
	0.3	++++	±	±	±
フアイナリン	0.1	++++	+++	+++	+++
	0.2	++++	+	++	+
	0.3	++++	±	±	±

但し各有機薬品の1日の服用量は次の如くである。

アンチピリン……0.6 g／日
バルビタール……0.6 g／日
アミノフイリン……0.6 g／日
ピラビタール……0.6 g／日
コントール……0.03 g／日
フアイナリン……0.12 g／日

以上より各生薬1日服用量に600mlの水を加えて調製した薬液、または有機薬品1日服用量に300mlの水を加えて調製した薬液への本発明で用いるウリジル酸、シチジル酸又はそのナトリウム塩の単独又は二種以上の混合物の添加量は0.2%以上に添加するのが好ましい。

次に実施例をあげる。

実施例　1

乾燥センブリ100gを粉砕して80メッシとし、これにCMP・2Na粉末800gを加えて良く混合してセンブリ0.15g／日の割合量に600mlの水を加えて加熱し煎じた後服用したが苦味は微弱であつた。

実施例　2

乾燥ゲンチアナ100gを粉砕し80メッシとしてこれにUMP・2Na 240gを加えて良く混合して、ゲンチアナ0.5g／日の割合量に600mlの水を加えて加熱して煎じた後服用したが苦味は微弱であつた。

実施例　3

アンチピリン粉末100gにUMP・2Na 66gとCMP・2Na 66gとを加えて混合し

7

てアンチピリン0.6g／日の割合量に300mlの蒸溜水を加えてよく溶して服用したが苦味は微弱であつた。

実施例　4

バルビタール粉末100gにCMP・2Na粉末132gを加えて良く混合してバルビタール粉末0.6g／日の割合量に300mlの蒸溜水を加えてよく溶して服用したが苦味は微弱であつた。

8

㊲特許請求の範囲

1　苦味を有する医薬品にウリジル酸またはシチジル酸、およびそのナトリウム塩の単独または二種以上の混合物を添加せしめることを特徴とする医薬品の苦味除去法。